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Among the entire group of factors which may exert an effect in space flight on living organisms the least well studied is the effect of factors related to life in airtight confined spaces, that is, directly related to the possibilities for future interplanetary flights.

As a result of increase of the duration of spacecraft flights the possibility of prolonged spacecraft habitation will not be limited by technical capabilities and the supplies of material goods but primarily by the tolerance of crew members and the physiological capability of man to remain a long time in the singular conditions of airtight enclosed spaces of limited volume. The most characteristic feature of habitation in an airtight cabin is the need for a prolonged stay of man under specific conditions of the environment: an artificial atmosphere, hypodynamia, isolation, etc.

In our experiments on human beings and on animals (rabbits, rats, mice) a study was made of the character of change of high-altitude tolerance in dependence on the rate of decompression, temperature and gas composition of the chamber and also the motor regime.

From the point of view of human physiology, modern spacecraft equipped with airtight cabins apparently completely solve the problem of flight in universal space. However, under real conditions it is impossible to neglect the possibility of air leakage from the cabin. Therefore, the study of the time that man retains work capacity at different rates of air decompression in the cabin assumes great importance. It was

established in experiments on human beings that the time of onset of decompression prior to the appearance of well-expressed functional disorders (difficulties in writing, darkening in the eyes, appearance of local convulsions, impairment of the rhythm of respiration, bradycardia, etc.) at a rate of ascent of 2 m/sec averaged 58 minutes and the altitude ceiling was 6,527 m. In the case of an ascent at a rate of 0.1 m/sec these values were as follows: 15 hours 21 minutes and 5,101 m respectively (Agadzhanyan, Zharov, Kuznetsov, Kalinichenko, Sergiyenko, et al, 1965). Having established for man the dependence of the change of the altitude ceiling and the reserve time on the decompression rate for two different decompression regimes, we decided to broaden the investigations in experiments on animals. In addition to the rates of 2 m/sec and 0.1 m/sec we also used other decompression rates (25, 75, 150, 300, and 500 m/sec). A total of 186 experiments were made. The results are given in Table 1, which clearly shows the dependence of the altitude ceiling and reserve time on the decompression rate.

Table 1

Change of Altitude Ceiling and Reserve Time for White Rats as a Function of the Rate of "Ascent" in a Pressure Chamber (Data of N.A. Agadzhanyan and A. V. Sergiyenko)

Decompression regime	No. of experiments	Altitude ceiling			Reserve time		
		min	max	mean	min	max	mean
2 m/sec	26	11700	14700	13370	105'35"	131'42"	121'32"
25 m/sec	30	13050	14325	13618	8'42"	9'33"	9'08"
75 m/sec	22	14150	16750	16088	3'08"	3'51"	3'32"
150 m/sec	38	17050	18900	18286	115"	130"	123"
300 m/sec	30	20000	22300	21495	67"	76"	72"
500 m/sec	40	24000	27200	25445	48"	55"	52"

The lesser the rate of ascent, the lower is the altitude ceiling and vice versa. However, if we consider the reserve time, we find that there is an inverse dependence: the slower the ascent is made, the greater is the reserve time. The data from investigation of the physiological reactions of the body revealed that in the case of rapid ascents a heavy load falls on the central nervous system, whereas in the case of slow ascents the load falls on the cardiovascular system. When the temperature in the chamber was 21° and the decompression rate was 2 m/sec the altitude ceiling was 13,370 m, and at 30° -- 10,221 m. When the temperature in the chamber was 21° and the decompression rate was 25 m/sec the reserve time at an

altitude of 12,000 m was 21 minutes, at 30° -- 4 minutes 25 seconds, at 40° -- 1 minute 39 seconds. We established a dependence between the change of altitude tolerance not only on the decompression rate and temperature in the pressure chamber, but also on the motor regime (hypo- and hyperdynamia).

The effect of hypodynamia on the body may be divided arbitrarily into two parts: changes in the body occurring directly at the time of prolonged limitation of muscular activity and the influence of the results of hypodynamia on different body functions. The first group includes: muscular atrophy and then atrophy of the bones, tightness of the joints (Gorinevskaya, 1938; Kudryavtseva, 1940).

As demonstrated by the experimental investigations of Agadzhanian and Kuznetsov and associates (1962), in the case of a 62-day stay of a man in an enclosed chamber of limited volume there was a decrease of the body consumption of oxygen and release of carbon dioxide. Dietrick, et al (1948) mention a decrease of basal metabolism during hypodynamia. At the same time there is a release with the urine of such elements as sodium, calcium, potassium, nitrogen, sulfur and phosphorus.

The second group of impairments includes a decrease of the tolerance of the body to the orthostatic effect (Taylor, et al, 1949; Lamb, Johnson, et al, 1964), accelerations, and large physical loads (Korobkov, 1961; Agadzhanian, Poruchikov, Kakurin, Kotovskaya, et al, 1964; Miller, Leverett, 1965).

Taylor mentions a decrease of the capacity of the respiratory and cardiovascular systems to provide a rapid supply of oxygen to the working tissues and a considerable increase of the amount of lactic acid in the body during muscular work after hypodynamia. However, the literature contains no data on the effect of hypo- and hyperdynamia on tolerance to hypoxia.

In experiments on animals we demonstrated that after a 25-day period of hypodynamia the altitude ceiling is decreased on the average by 2,707 m, whereas after daily physical training (swimming) it increases. Data on the change of the altitude tolerance of rats after 10- and 25-day periods of hypodynamia are given in Table 2 and in Figures 1 and 2.

Clarification of the effect of prolonged breathing of high oxygen concentrations on the subsequent tolerance to acute hypoxia (simulation of impairment of the intactness of the airtight cabin) also is of great practical importance.

Table 2

Character of Change of Altitude Tolerance of Rats After 10- and 25-Day Periods of Hypodynamia (Rate of Ascent 25 m/sec)

Test	Altitude of appearance of convulsions		Difference between control and 25-day hypodynamia	Altitude ceiling			Difference between control and 25-day hypodynamia
	control	10 days	25 days	control	10 days	25 days	
1	13500	13000	10000	13925	14000	12150	1774
2	13300	12300	10500	13750	13800	11700	2050
3	12600	11800	11500	13375	13100	11500	1875
4	12800	12400	12400	13525	13550	12400	1125
5	13100	12800	13000	13625	13900	13800	+175
6	12700	13500	12300	13750	14100	12500	1250
7	12500	13300	12100	13300	13700	12900	400
8	12800	13200	10900	14050	14100	11200	2850
9	13000	13200	11500	14325	13650	12700	1625
10	13200	12500	died	14300	13300	died	-
Mean	12950	12800	10420	13792	13720	11085	2707

These experiments revealed that in the case of a prolonged (up to 10 days) stay of animals in an atmosphere containing high O_2 concentrations (pO_2 720 and 405 mm Hg) on the first day the reserve time at an altitude of 12,000 m is greater than at the initial level, but on the days which follow, on the other hand, the tolerance to hypoxia is reduced sharply as a result of the toxic effect of oxygen (Figures 3 and 4).

A particularly well-expressed decrease of altitude tolerance is observed immediately after replacement of a medium with a high oxygen content by the ordinary atmosphere. The reserve time at an altitude of 12,000 m in this case is reduced to 1.5 minutes, whereas the initial data indicate an average of 11.5 minutes. These data can be used in developing a number of scientifically sound prophylactic measures for ensuring the safety of flights of modern spacecraft, in particular, in developing emergency methods for rescuing a crew for different rates of leakage of the atmosphere from the airtight cabin.

Although a large number of basic studies have been devoted to the effect of oxygen deficiency on the body, our knowledge on this problem is far from complete and many problems still remain unsolved. For example, whereas a thorough study has been made of adaptive reactions directed to maintaining a constancy of partial pressure in the blood and to an increase of utilization of oxygen by the tissues, we still know little about changes of tissue metabolism under the influence of hypoxia. We also know little about the change of the vital activity of different functional systems of the body and physiological mechanisms of impairments, particularly the functions of the higher parts of the brain arising under the influence of hypoxia. It has been established that the dynamics of change of the bioelectric activity of the brain under the influence of hypoxia passes through three stages: predominance of rhythms of excitation (from an altitude of 1,000 m), a dominance of slow-wave activity (from an altitude of 8,000 m) and from an altitude of 11,000-12,000 m there is a suppression of electrical activity up to complete attenuation (Livonov and Parfenova, 1945; Malkin, Razumeyev and Izosimov, 1965; Motoboyashi, Mitaran, Ando, 1963; Gezalyan, Il'in, Razumeyev, 1966 and others).

The dynamics of conditioned reflex activity under the influence of hypoxia is more complex. The first changes of the conditioned reflexes are observed at altitudes of 1,000-3,000 m (shortening of the latent period, increase of the expression of the conditioned reflexes and unconditioned salivation) and at great altitudes (4,000-6,000 m) the animals usually mani-

fest phase states (Lifshits, 1949; Zvorykin, 1951; Altukhov, 1952; Mal'medzhak and Plein, 1951 and others). At altitudes of 6,000-7,000 m alimentary conditioned reflex reactions completely disappear but defense reflexes remain (Agadzhanian, 1956). Thus, the disappearance of conditioned reflexes occurs even while a stage of excitation remains on the EEG. These changes of conditioned reflex activity are attributed by the authors to impairment in the initial stages of the processes of conditioned inhibition and in the subsequent development of protective inhibition.

In the absolute majority of the investigations made on animals the recording of the EEG and the conditioned reflex method were used separately at the time of hypoxia for study of cerebral functions. Under conditions of free movement of the animals we attempted to combine study of conditioned reflex activity with a simultaneous investigation of changes of the EEG under the influence of hypoxia, that is, establish a correlation of the changes of the bioelectric activity of the brain and the conditioned reflex activity.

The experiments were made on six rabbits with the recording of biopotentials under conditions of free movement, from the visual region of the cortex of the lateral field of the hypothalamus, dorsal hippocampus and reticular formation of the midbrain. In all the animals we produced a conditioned alimentary reflex to a rhythmic light stimulus (5 flashes per second) and negative differentiation (3 flashes per 2 seconds). With a strengthened reflex the reaction of assimilation of the rhythm of the stimulus was registered in the cortex and in the lateral field of the hypothalamus (hunger center -- Anand, 1954, and others) and was absent in the other studied leads.

When the animals in the pressure chamber ascended at the rate of 25 m/sec it was noted that at an altitude of about 3,000 m an alleviation of the conditioned alimentary reflexes began and there was an increase of the intersignal alimentary movements, which correlates with the appearance of an intersignal manifestation of the reaction of assimilation of the rhythm of the signal on the EEG of the lateral field of the hypothalamus. This indicates an increase of excitation of the anterior-lateral parts of the hypothalamus at these altitudes, which may explain the alleviation of the conditioned reflexes of the animals, and in human subjects -- manifestations of euphoria and exaltation (Sirotnin, 1954).

At altitudes of 5,000-7,000 m the conditioned alimentary reflexes disappeared and the EEG showed a compulsive reaction not only in the cortex and hypothalamus, but also in the

reticular formation of the midbrain (generalization), which is evidence of a change of the biological significance of the transmitted signal and an increase of excitation of the non-specific system of the brain stem.

With a further ascent we recorded a paradoxical and a transforming stage of parabiosis (Ukhtomskiy), which is expressed in the appearance of a change with a frequency of the biopotentials of 2 oscillations/sec on the EEG of the hypothalamus and reticular formation in response to light flashes with a frequency of 5 per second and retention of the ordinary compulsive reaction in the visual zone of the cortex and also assimilation with a frequency of 2 per 3 seconds, which was not observed prior to the ascent. Beginning at altitudes of 8,000-10,000 m the EEG shows slow waves and compulsive reactions are not apparent in the structures of the subcortex (inhibition phase of parabiosis), but are retained in the visual region of the cortex.

These experiments revealed that as ascent continues there are at least two qualitative stages of change of the behavior of the animals in conditioned reflex activity and on the EEG: one at an altitude of 3,000 m, where there is an alleviation of the conditioned reflexes, and a second at an altitude of 6,000 m, where the alimentary reflexes disappear but the defense reflexes remain. Rhythms of excitation dominate on the EEG at this time. In a special series of experiments we made a quantitative evaluation of the changes of the EEG, and in particular we devoted attention to changes of the energy of the delta waves (determined using an integrator) because the decrease of the latter was evidence of a shift of the EEG frequency to the right, that is, an increase of excitation (Zayler and Stumpf, 1958; Kalyuzhnyy and Kotlyar, 1966, and others). Determinations of this energy revealed that with ascent at a rate of 25 m/sec at an altitude of 3,000 and 6,000 m there is a reliable decrease of the energy of the delta waves in the range 25-50% of the initial level (Fig. 5). This is evidence that at these altitudes there is an increase of the excitation of the structures of the brain, with which the above-mentioned change of higher nervous activity is correlated.

We also made a pharmacological analysis of the above-mentioned changes of the EEG. It was found that the injection of scopolamine annuls the increase of excitation at an altitude of 3,000 m, but not at 6,000 m. The injection of aminazin caused the opposite effect.

Thus, the intensification of excitation of the cerebral

subcortical formations arising at altitudes of 2,000-3,000 m is associated with a predominance of excitation of the cholinergic system of the brain, particularly the anterior-lateral parts of the hypothalamus, probably as a result of increase of the flux of impulses from the chemo- and baroreceptors. At altitudes of 5,000-7,000 m there is a second qualitative intensification of excitation which is associated with a predominance of the function of the adrenergic system of the brain, particularly the reticular formation of the brain stem and the hypothalamus, as a result of which there is a change of the biological significance of the conditioned stimulus and there is a generalization of the rhythms of compulsiveness, the alimentary reflexes disappear and the defense reactions of the animals predominate. At great altitudes the development of phases of parabiologic states occurs, which is expressed on the EEG by the appearance of slow waves, as a result of cutting off of the activating system of the brain stem.

In order to develop measures ensuring an increase of altitude tolerance we organized and carried out three high-mountain scientific expeditions to the Central Tien Shan.

It was demonstrated, in particular, that with gradual acclimatization in the mountains altitude tolerance increases. The reserve time of the animals at an altitude of 12,000 m by the fifteenth day of acclimatization increases on the average by 32%, and by the 25th-30th day -- by 76%. In the experiments with human subjects and with animals it was established that the minimum time for mountain acclimatization is 26-28 days.

Also established was a dependence of the change of altitude tolerance not only on environmental conditions, but also on time of day and change of season.

These experimental data indicate that it is necessary to create an optimal environment within the spaceship cabin and organize a rational work and rest schedule.

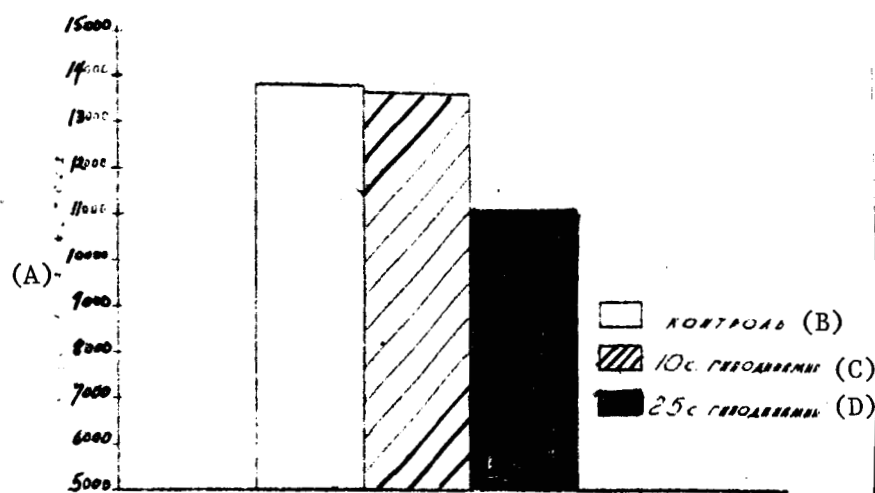


Fig. 1. Change of altitude ceiling for rats as a function of duration of hypodynamia (rate of ascent 25 m/sec). A) Altitude in meters; B) Control; C) 10 days of hypodynamia; D) 25 days of hypodynamia.

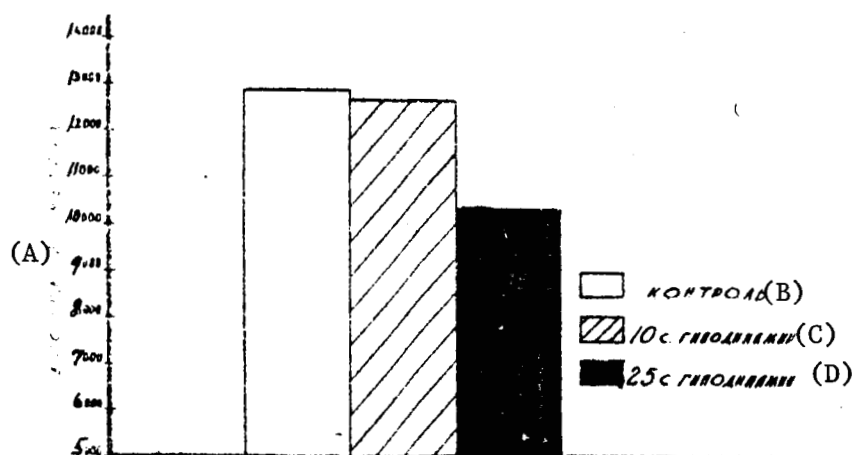


Fig. 2. Change of "altitude" of appearance of convulsions in rats as a function of duration of hypodynamia (rate of ascent 25 m/sec). A) Altitude in meters; B) Control; C) 10 days of hypodynamia; D) 25 days of hypodynamia

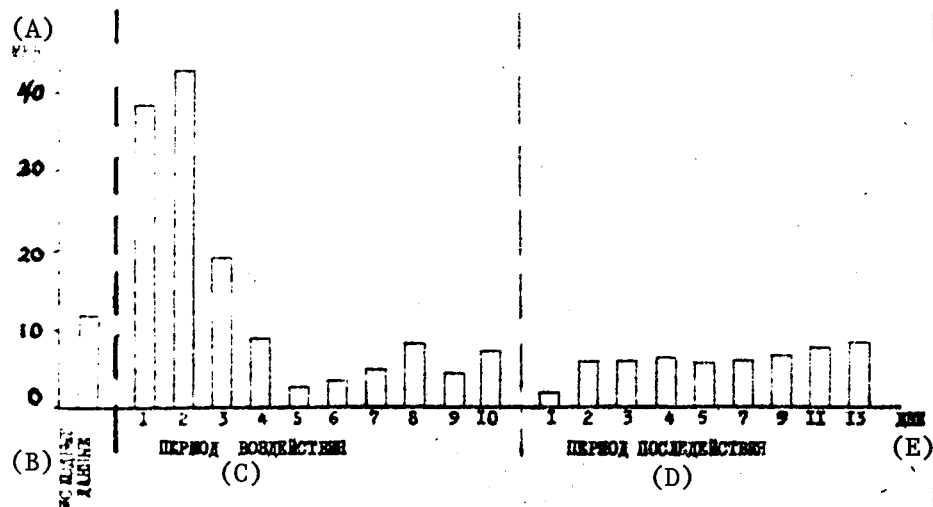


Fig. 3. "Reserve time" at altitude of 12,000 m after different periods of presence in an atmosphere containing 90% O₂. A) min; B) Initial data; C) Period of effect; D) Period of aftereffect; E) Days.

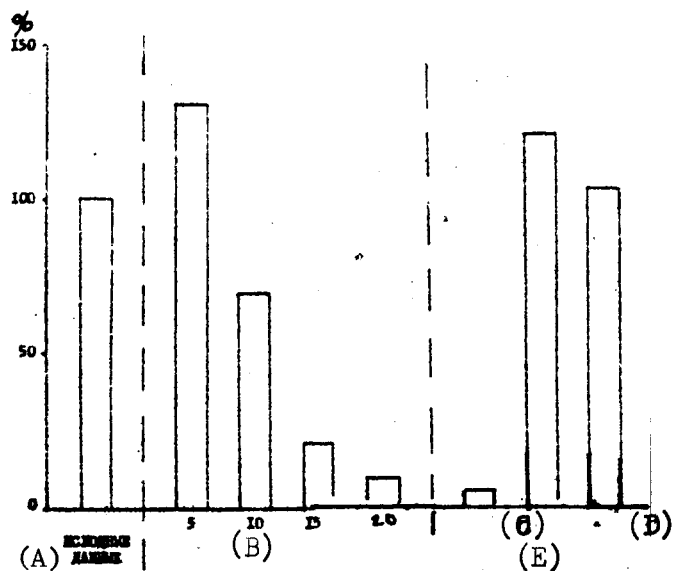


Fig. 4. "Reserve time" at altitude of 12,000 m (in % of initial level) after different periods of presence in an atmosphere containing 53% O₂.

A) initial data; B) Period of Effect; C) (Translator's note): Illegible; D) Days; E) Period of Aftereffect.

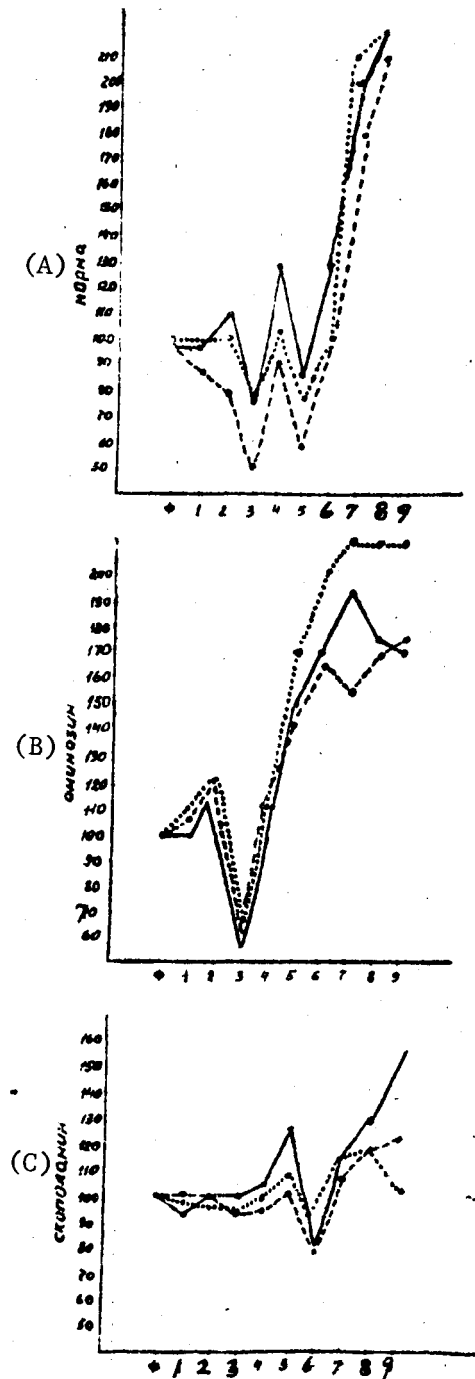


Fig. 5. Dynamics of changes of energy of delta waves of EEG at different altitudes (in % of initial level). Along x-axis -- altitude in km; along y-axis -- energy of delta waves. Solid line: cortex; dashed line: reticular formation; dotted line: hypothalamus. A) Normalcy; B) Aminazin; C) Scopolamine.